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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,947	12/12/2005	James N. Petitte	297/204 PCT/US	1436

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EXAMINER
WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,947	PETITTE ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-10 and 12-57* is/are pending in the application.

4a) Of the above claim(s) *12-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-9-09 has been entered.

Claims 5, 6 and 11 have been canceled. Claims 1-4, 7-10 and 12-57 remain pending.

Election/Restrictions

This application contains claims 12-57 drawn to an invention nonelected with traverse in the reply filed on 6-18-07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-4 and 7-10 are under consideration as they relate to decreasing PGC numbers/development using DAZL proteins.

Applicant's arguments filed 4-9-09 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The IDSs filed 4-9-09 and 4-14-09 have been considered, but certain citations have been lined through that cannot go onto the front page of a published Patent.

Claim Objections

Consider: –i) immunizing a female bird with DAZL, ii) obtaining an egg comprising an embryo from the female bird, wherein the egg comprises antibodies that recognize DAZL in an amount sufficient to bind to DAZL on PGCs of the embryo and decrease the number of PGCs in the embryo, iii) repopulating the gonad of the embryo with donor PGCs of a different strain of the same species, and iv) obtaining a chimeric avian from the embryo.-- Please point to support for each step in the specification originally filed upon amendment.

Claim Rejections - 35 USC § 112

New Matter

The rejection of claims 1-4 and 7-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in view of the abstract originally filed and the paragraph bridging pg 11-12.

Enablement

I. Claims 1-4 and 7-10 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is drawn to a method for modulating primordial germ cells (PGC) numbers in an avian embryo, the method comprising immunizing a female bird with an antigen associated with primordial germ cells, whereby an egg produced by the female bird comprises a sufficiently high concentration of antibodies specific for the antigen to bind to the antigen expressed by an avian embryo within the egg to decrease endogenous PGC numbers in the avian embryo. Claim 7 is drawn to a method for modulating primordial germ cells (PGC) development in an avian embryo, the method comprising immunizing a female bird with an antigen associated with primordial germ cells, whereby an egg produced by the female bird comprises a sufficiently high concentration of antibodies specific for the antigen to bind to the antigen expressed by an avian embryo within the egg to inhibit development of PGCs in the avian embryo.

A. Claims 1 and 7 encompass decreasing PGCs in an avian embryo without repopulating the embryo with donor PGCs and without obtaining a chimeric avian. However, the sole disclosed use for decreasing PGCs in an avian embryo is to repopulate the embryo with donor PGCs and make chimeric avians (pg 1, lines 14-30; paragraph bridging pg 2-3; pg 36, lines 4-11). Accordingly, repopulating the embryo with donor PGCs and obtaining a chimeric avian are essential steps to the method

claimed. The specification teaches decreasing PGC numbers in an embryo using DAZL-C and DAZL-N proteins administered to female chickens (pg 55, lines 19-26; pg 56, lines 12-17). The number of PGCs was determined by sacrificing the embryo (pg 54, lines 4-6). While the specification exemplifies the step of decreasing PGCs without repopulating the embryo with donor PGCs and obtaining a chimeric embryo, the specification does not teach how to decrease PGCs in an embryo that is sacrificed as described on pg 54. Without such guidance, applicants fail to provide an enabled use for merely decreasing PGCs and sacrificing the embryo as described on pg 54-56. Overall, the specification does not provide an enabled use for merely decreasing PGCs in an avian embryo as claimed without repopulating the treated embryo with donor PGCs and without obtaining a chimeric avian.

Applicants argue paragraph 6 of the Declaration by Dr. Petitte filed 4-9-09 shows methods of decreasing PGC numbers were known in the art. Applicants' argument is not persuasive. The specification and the art at the time of filing do not provide an enabled use for merely destroying PGCs in an embryo and sacrificing the embryo without obtaining a chimeric avian.

B. Applicants have provided no means for assaying whether PGC numbers decrease in an embryo that becomes a viable avian. Specifically, applicants fail to teach how to determine whether amounts of antigens or antibodies that decrease endogenous PGC numbers had been injected or obtained as claimed without sacrificing the embryo. This is essential to the invention as the sole disclosed use for the method claimed is to obtain a chimeric avian from the embryo (see section A above). The

specification teaches assaying the number of PGCs in an embryo in the egg of an avian treated with DAZL-C and DAZL-N (pg 55, lines 19-26; pg 56, lines 12-17) by sacrificing the embryo (pg 54, lines 4-6). However, the specification fails to teach how to determine PGC numbers while letting the embryo survive. The ability to predict whether PGC numbers had decreased after immunizing an avian with an antigen was not described at the time of filing or in the specification; therefore, the ability to do so is "unpredictable." The specification fails to teach how to use the assay in which the embryo is sacrificed on pg 54 to determine whether PGC numbers decreased in a viable avian.

In addition, the specification does not teach how to use breeding techniques to assay PGC numbers. A chimeric avian obtained from the embryo could be bred, and if donor PGCs were administered to the embryo, it could be determined whether the donor PGCs had repopulated the gonad by observing for donor PGC phenotypes in the offspring. The specification, however, does not teach any such assay. The specification does not teach how to use breeding techniques to determine that a decrease in PGC numbers had occurred. In particular, such a technique could not apply to chimeric interspecies avians; such a technique would require counting the number of chickens and turkeys that occur from breeding a chimeric chicken/turkey which is not disclosed in the specification or the art at the time of filing. Such a technique could not apply to avians made with donor PGCs of the same strain; the specification does not teach how to distinguish donor PGCs and endogenous PGCs of the same strain during breeding assays.

Overall, the specification has left those of skill with undue experimentation to determine whether PGC numbers decreased in an avian embryo as claimed without sacrificing the embryo.

Applicants argue the techniques disclosed for visualizing PGC numbers in ovo can be used on a subset of treated animals, and the results of the tests performed on these avians can be extrapolated with a high degree of predictability to similar treated avians that are permitted to hatch. Applicants' argument is not persuasive. Such a method is not explicit or implicit from the specification as originally filed. Furthermore, the ability to decrease PGC numbers by immunizing an avian with an antigen was unknown at the time of filing; the predictability of doing so is not disclosed by applicants as being “high” or able to be extrapolated. Accordingly, it is not readily apparent that results in one avian extrapolate to other avians. Applicants have provided no means for assaying whether PGC numbers decreased before repopulating the embryo with donor PGCs. Applicants have provided no means for assaying whether PGC numbers decrease in an embryo that becomes a viable chimeric avian.

Applicants argue the degree of chimerism is easily assayable by breeding the chimeric avian. Applicants’ argument is not persuasive. Such an assay is not disclosed in the specification. Furthermore, the specification does not teach when the degree of chimerism indicates a decrease in PGC numbers had been obtained. Next, applicants do not teach how to obtain a chimeric interspecies avian as encompassed by the claim, so those of skill would not be able to perform the assay when the donor PGCs were of a different species than the embryo. Finally, when the donor PGCs are the same species

and strain as the recipient embryo, there is no "degree of chimerism." Overall, applicants have failed to provide a means of testing whether PGC numbers decreased in an embryo that becomes a viable avian.

C. The specification does not enable repopulating an avian embryo with PGCs from another avian species. The specification suggests the donor PGCs are from different species than the recipient embryo (pg 4, lines 24-27). The specification and the art at the time of filing did not teach how to obtain a viable chimeric avian made from two different avian species. The specification and the art at the time of filing did not teach how to use a method that merely results in a chimeric embryo made from two different species that does not survive. Without such guidance it would have required those of skill in the art at the time the invention was made undue experimentation how to use an interspecies embryo that does not survive made by the method claimed or how to use the method claimed to make a viable chimeric interspecies avian.

Applicants point to Exhibit G, a graduate thesis from 1999 in which chicken PGCs were introduced into a turkey embryo. Applicants appear to argue the art at the time of filing enables implanting PGCs from another species into chicken embryos. Applicants' argument is not persuasive. Exhibit G does not teach how to use the interspecies embryo that does not survive or how to make a viable chimeric interspecies avian. Survival of the chimera remains essential to applicants' invention. One test for whether the chimeric offspring in Exhibit G was a germline chimera would be to obtain a turkeys/chicken chimera from the offspring and determine whether it was capable of giving rise to both chickens or turkeys; however, this is not disclosed in Exhibit G, in

applicants' disclosure or anywhere in the art at the time of filing or since. Exhibit G required sacrificing the chimeric embryos, which does not have an enabled use in the instant application.

D. The specification does not enable repopulating an avian embryo with PGCs from the same strain of avian. The specification suggests the donor PGCs are from the species than the recipient embryo (pg 4, lines 24-27). The specification and the art at the time of filing do not provide a use for such an embryo or for a viable avian obtained from such an embryo. The specification and the art at the time of filing do not teach how to assay and determine PGC numbers decreased in such an embryo when they are repopulated with PGCs from the same species. The specification and the art at the time of filing do not teach how to distinguish endogenous and donor PGCs when they are of the same strain of avian. Accordingly, it would have required those of skill undue experimentation to determine how to do so.

E. The specification does not enable using any antigen "associated" with PGCs as broadly claimed. Claims 1 and 7 require administering "antibodies specific for the antigen to bind to the antigen expressed by an avian embryo within the egg to thereby decrease endogenous PGC numbers". The specification defines antigens "associated" with PGCs as any antigen expressed by a PGC (paragraph bridging pg 11-12). The claims encompass antigens associated with PGCs and any other cells; the claims encompass antibodies attacking the antigen expressed on PGCs and anywhere else in the avian embryo. For example, the claim now encompasses using a histocompatibility marker present on all cells (and also "associated" with PGCs) as the

antigen. The claims also encompass binding the antibodies to antigen anywhere in the embryo. Pg 29 states "antibodies that bind antigens associated with PGCs are deposited in the yolk of eggs produced by female birds immunized with the antigen." Pg 30-31 discusses modulating PGC development in an avian embryo. The examples, however, are limited to using antigens that are specific to PGCs. The specification does not teach how to use the method claimed when the antigen is "associated with" PGCs and other embryonic cells as now broadly claimed. Without using antigens that are specific to PGCs, the antibodies obtained in the egg would destroy all tissues expressing the antigen and prevent survival of the embryo. Applicants fail to adequately teach how to use the method claimed with any antigen "associated with" PGCs that would also destroy tissues other than PGC in the embryo. Without such guidance, it would have required those of skill undue experimentation to determine how to administer any antigen "associated with" PGCs such that destruction of non-PGC tissues in the embryo is prevented and survival of the embryo is allowed.

Indefiniteness

II. Claims 1-4 and 7-10 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The metes and bounds of what applicants consider "sufficiently high concentration of antibodies specific for the antigen to bind to the antigen expressed by an avian embryo within the egg to thereby decrease the PGC numbers [or development] in an avian embryo" (claims 1 and 7 as amended) remain unclear. The specification

does not teach how to determine whether PGCs numbers decrease without sacrificing the avian (pg 54, lines 4-6, "Stage 27 (H&H) embryos were sacrificed"). The specification does not teach how to use the assay on pg 54 when making chimeric avians (the sole disclosed use for the method claimed). The concentration of antibodies required to decrease the number or development of PGCs and maintain a viable embryo is not set forth in the specification or the art at the time of filing. Applicants have not provided an assay for those of skill to determine when the amounts of antibodies were "sufficiently high" enough to decrease PGC numbers in an embryo that becomes a viable avian. Thus, those of skill would not be able to determine when the concentration of antibodies obtained was infringing on the claim when making viable chimeric avians.

In response to the rejection, applicants summarize the invention (pg 17-18) and conclude those of ordinary skill in the art could easily determine the amount of antibodies in an egg of the avian required to specifically bind PGCs of the embryo and decrease the number of PGCs in the embryo. Applicants argue one of ordinary skill could determine if they are infringing on the claim by breeding the chimeric embryo once they reach sexual maturity. Applicants' arguments are not persuasive. Applicants have not pointed to the amount of antibody in an egg produced by an avian required to decrease PGC numbers in an embryo in the egg. The claims do not require obtaining a chimeric avian from the embryo. In fact, the claims encompass repopulating the embryo with donor PGCs of the same strain – it is wholly unclear how breeding would reveal whether PGC numbers decreased in such avians. More importantly, the specification does not teach how to breed avians to determine whether antibody levels

were "sufficiently high". Applicants have not pointed to one specific assay that would reveal whether the amount of antibody obtained in the egg of the avian was "sufficiently high" to bind the antigen on PGCs and decrease the number of PGCs in the embryo as claimed in a manner that allowed the embryo to survive.

Applicants argue those of skill would be able to predict whether PGC numbers had decreased in an embryo because the antibody production against such antigens was predictable and results obtained in one avian could be extrapolated to another. Applicants' argument is not persuasive. No such predictability is apparent from the specification or the art at the time of filing. No such assay is disclosed or readily apparent in the specification.

Applicants argue the Examiner has constructed artificial requirements for interpreting the claims. Applicants assert those of skill would have understood the metes and bounds of when antibody levels were "sufficiently high" as claimed. Applicants' argument is not persuasive. Applicants have not taught the amount of antibodies required to bind PGCs and decrease PGC numbers in an embryo and have not provided the assays required to determine the antibody levels required to bind PGCs and decrease PGC numbers in an embryo. Accordingly, the metes and bounds of the amount of antibody required to meet the limitation claimed cannot be determined.

B. The metes and bounds of what applicants consider antibodies "specific for the antigen to bind to the antigen expressed by an avian embryo within the egg to thereby decrease endogenous PGC numbers" (claims 1 and 7) are unclear. It cannot be determined how specific the antibodies must be to decrease endogenous PGC

numbers. The specification and the art at the time of filing provide no guidance in this regard. The phrases "to bind" and "to thereby decrease endogenous PGC numbers" are intended uses that may not occur. Accordingly, those of skill would not be able to determine whether antibodies that recognized any DAZL antigen, for example, was encompassed by the claim of if the phrase was limited to antibodies that are specific to a particular DAZL antigen, i.e. DAZL-C or DAZL-N.

Applicants argue the claimed method takes advantage of the ability of a female avian to make antibodies in its eggs that bind PGCs. Applicants' argument is not persuasive because applicants have not taught how specific the antigen must be to decrease PGC numbers in the embryo.

Applicants argue the examiner is basing the rejection on functional language without interpreting the language in context of the claim as one of ordinary skill in the art. Applicants' argument is not persuasive. The specification and the art do not teach how specific the antibodies must be to the antigen to decrease PGC numbers. In addition, the phrase "to bind to the antigen expressed by an avian embryo within the egg to thereby decrease endogenous PGC numbers" contains two intended uses that do not have to occur and is not written to clearly describe the function of the antibodies.

Applicants argue the language relates to an outcome – the decrease in PGCs. Applicants' argument is not persuasive. As written, the outcome is not directly linked to the antigen or the antibodies. The claims do not clearly set forth administering an antigen to an avian embryo, wherein the antigen is specific to avian PGCs, such that endogenous PGC numbers in the avian embryo decrease. The claims do not clearly

set forth administering an antigen to an avian embryo, such that antibodies that recognize the antigen are obtained, wherein the amount of antibodies obtained are sufficient to decrease endogenous PGC numbers in the avian embryo. Thus, the claims as amended remain unclear how the specificity of the antibodies to the antigen relates to the outcome.

The art did not reasonable teach or suggest modulating primordial germ cells (PGC) numbers/development in an avian embryo by immunizing a female bird with an antigen associated with primordial germ cells, whereby an egg produced by the female bird comprises a sufficiently high concentration of antibodies specific for the antigen to decrease the number of PGCs or inhibit the development of PGCs in an avian embryo present within in the egg.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner